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Tanruprubart, Anti-C1q Therapy, Accelerates Recovery and Reduces Ventilation in Severe Guillain-Barré Syndrome: Results From the Phase 3 GBS-02 Trial

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Presented by Pallavi Lacey[1] on behalf of the authors

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Introduction

- Guillain-Barré syndrome (GBS) is a severe, life-altering, autoimmune disorder mediated by classical complement affecting peripheral nerves, resulting in muscle weakness and often prolonged recovery[1]
- Patients may need intensive care unit (ICU) admission, with approximately 25% progressing to respiratory failure requiring mechanical ventilation.[1–3] Patients can experience persistent disability, including being unable to walk after 6 months[1–3]
- Tanruprubart (ANX005), a monoclonal antibody, is a targeted immunotherapy that selectively binds to and inhibits C1q, the initiating molecule of the classical complement pathway, thus providing rapid inhibition of complement-mediated neuroinflammation and nerve damage[4,5]
- Tanruprubart was evaluated in GBS-02 (NCT04701164), a Phase 3, multicentre, double-blind, placebo-controlled trial in patients with GBS[6]
- Here we present the prespecified measures of clinical benefit associated with patient recovery time and resource utilisation

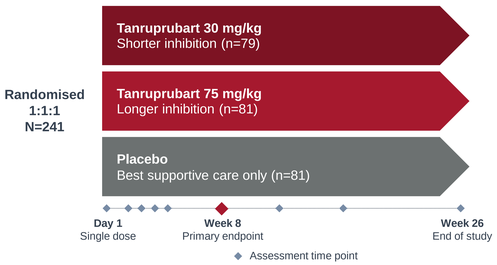
Methods

GBS-02 study design

Key inclusion/exclusion criteria:
- Aged ≥16 years
- With a GBS-DS of 3, 4, or 5
- ≤10 days from onset of weakness
- Did not have access to intravenous immunoglobulin or plasma exchange

Stratified by baseline prognostic factors: muscle strength and time from onset of weakness

Conducted at sites in Bangladesh and the Philippines



Primary endpoint:

- **GBS-Disability Score** (GBS-DS) at Week 8

Key secondary endpoints included:

- **Muscle Strength,** assessed by Medical Research Council sumscore (MRCss) change from baseline at Weeks 1 and 8
- **Time to walking independently,** assessed by GBS-DS ≤2, analysed using time-to-event methods
- **Duration of mechanical ventilation,** assessed using the zero-inflated negative binomial (ZINB) model and imputed for death. To avoid underestimation of ventilator burden for participants who died while on mechanical ventilation, they were assigned 182 days (the full trial length)
- **Duration of ICU stay,** assessed using the ZINB model. To avoid underestimation for participants who died, duration of ICU stay was imputed to 182 days (full trial length), regardless of the need for or actual duration of ICU stay

Results

- The study met the primary endpoint and demonstrated that patients treated with tanruprubart 30 mg/kg had better outcomes (adjusted odds ratio 2.4, 95% CI 1.3–4.5; p=0.0058) according to the GBS-DS relative to placebo at Week 8 (**Figure 1**)
  - The p-value for the primary endpoint is statistically significant. Other reported p-values are nominal
- Rapid improvements in muscle strength (MRCss) with tanruprubart 30 mg/kg versus placebo were observed as early as Week 1 (**Figure 2**)
- Patients who received tanruprubart 30 mg/kg could walk independently a median of 31 days earlier compared with patients who received placebo (p=0.0211; **Figure 3**)
- The duration of mechanical ventilation was a median 28 days less compared with placebo (p=0.0356; **Figure 3)**
- The median ICU stay for the tanruprubart group was 7 days less than the placebo group (p=0.5306; **Figure 3**)
- Tanruprubart was well tolerated, and most adverse events were mild to moderate in severity, attributed to GBS, and not considered related to the study drug

Figure 1. GBS-02 primary endpoint: Change in GBS-DS at Week 8

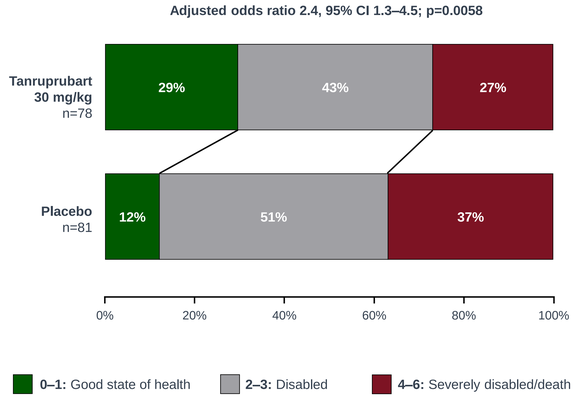
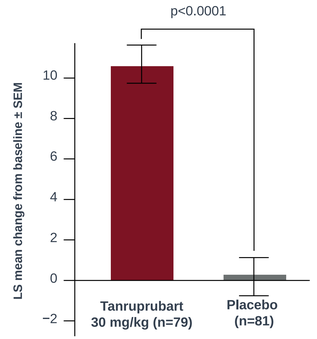
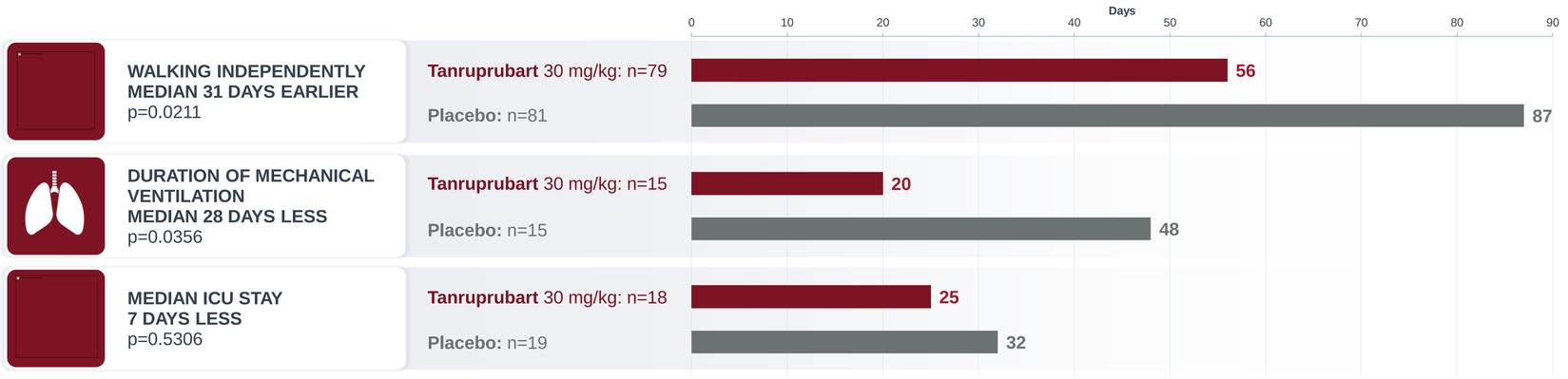


Figure 2. Recovery in muscle strength (MRCss) at Week 1



LS: Mean point improvement relative to placebo.
LS, least squares; SEM, standard error of the mean.

Figure 3. Walking independently, median ICU stay, and duration of mechanical ventilation with tanruprubart 30 mg/kg vs placebo



CONCLUSIONS

- In this Phase 3 study of severe GBS, tanruprubart improved recovery-related outcomes, including earlier independent walking and shorter ventilation duration, with the possibility of shorter time in the ICU, consistent with clinically meaningful benefit
- Targeted classical complement inhibition with tanruprubart has the potential to improve critical clinical outcomes in GBS

References

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Disclosures

H-AK, EP, PL: Employees and shareholders of Annexon Biosciences. GM: Employee and shareholder of Annexon Biosciences at the time of the study. QDM: Consultancy/advisory role with Annexon Biosciences, argenx, Janssen, and Sanofi. For additional information, please contact Henk-André Kroon: hakroon@annexonbio.com.